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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,604	07/01/2003	Wei Huang	011068-014-999	4803
20583	7590	09/22/2004	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			CHEN, STACY BROWN	
			ART UNIT	PAPER NUMBER

1648

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/612,604

**Applicant(s)**

HUANG ET AL.

**Examiner**

Stacy B Chen

**Art Unit**

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/04; 4/04; 5/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's election without traverse of Group I, claims 1-19, in the reply filed on July 30, 2004 is acknowledged. Claims 1-20 are pending. Claims 1-19 are under examination. Claim 20 is withdrawn from consideration being drawn to a non-elected invention.

#### ***Information Disclosure Statement***

2. The information disclosure statements filed on April 30, 2004, May 19, 2004 and July 2, 2004 have been considered.

#### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 14, 17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 12, 14, 17 and 19 recite a method for determining whether a human immunodeficiency virus type 1 (HIV-1) has an increased likelihood of having an impaired replication capacity. The method steps comprise: detecting whether the reverse transcriptase encoded by said HIV-1 exhibits the presence or absence of a mutation associated with impaired replication capacity. The mutation occurs at position 236 in said reverse transcriptase; specifically, the mutation is P236L. However, claims 12, 14, 17 and 19 ultimately depend from claim 1 which specifically prohibits the mutation P236L. This appears to be contradictory and requires correction.

*Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Whitcomb (WO 99/61658). The claims are drawn to a method for determining whether an HIV-1 has an increased likelihood of having an impaired replication capacity<sup>1</sup>. The method steps comprise: detecting whether the reverse transcriptase (RT) encoded by said HIV-1 exhibits the presence or absence of a mutation associated with impaired replication capacity. The mutation occurs at position 98, 100, 101, 103, 106, 108, 179, 181, 188, 190, 225 or 236 (not mutation P236L) in said reverse transcriptase. (The reference amino acid sequence for the reverse transcriptase is from HIV NL4-3, Genbank AF324493, see page 12 of the specification.) Specific substitution mutations are A98G, L100I, K101E, K103N, V106A, V106I, V106M, Y181C, Y188A, Y188C, Y188H, Y188L, G190A, G190C, G190E, G190T, G190V, G190Q, G190S, G190V, P236L and P225H. The mutation confers resistance to a non-nucleoside reverse transcriptase inhibitor, such as nevirapine, delavirdine or efavirenz. Also claimed is a method for determining whether a subject has an HIV-1 with an increased likelihood of having an impaired replication capacity. The subject is undergoing or has undergone prior

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<sup>1</sup> A virus has an “increased likelihood of having an impaired replication capacity” if the virus has a property, in this case, a mutation, correlated with an impaired replication capacity. The specification (page 10, lines 27-29) states that, “[A] property of a virus is correlated with an impaired replication capacity if a population of viruses having the property has, on average, an impaired replication capacity relative to that of an otherwise similar population of viruses lacking the property.”

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treatment with an antiviral drug. Various combinations of mutations are claimed in claims 10-19. Note that claims 1, 5 and all respective dependent claims exclude the mutation P236L, however, claims 12, 14, 17 and 19 recite the mutation P236L, see 35 U.S.C. 112, second paragraph rejection above. For purposes of compact prosecution, the positive recitation of the mutation P236L has been searched.

Whitcomb discloses means and methods for monitoring non-nucleoside reverse transcriptase inhibitor anti-retroviral therapy, specifically HIV therapy (abstract).

Whitcomb discloses substitution mutations in HIV-1 reverse transcriptase at codons 101, 103 and/or 109 that correlate with changes in delavirdine, nevirapine and efavirenz susceptibility (page 12, lines 4-25). Also taught is that mutations at codons 106, 189, 181 and/or 227 of HIV-1 reverse transcriptase result in decreased susceptibility to delavirdine, nevirapine and efavirenz. Another embodiment of Whitcomb's invention is that a mutation at codon 190 (G190A) either alone or in combination with a mutation at codon 130 (K103N) of HIV-1 RT correlates with resistance to antiretroviral therapy (page 14, lines 29-34), which meets the limitations of instant claims 11, 12, 16 and 17. Another embodiment of Whitcomb's invention is that a mutation at codon 236 (P236L) either alone or in combination with mutations at other codons including 103 (K103(N) and/or 181 (Y181C) of HIV RT correlates with resistance to antiretroviral therapy (see description of figures 5 and 6, pages 22-23), which meets the limitations of instant claims 13, 14, 18 and 19. Therefore, the claims are anticipated by Whitcomb.

5. Claims 1-13 and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Richman *et al.* (*J. Virology*, March 1994, 68(3):1660-1666, herein, "Richman"). The

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claims have been summarized above. Richman discloses non-nucleoside reverse transcriptase (RT) resistance mutations of HIV-1 RT: 100, K103N, V106A, Y181C, V108I, Y188L, G190A, 236 and others (abstract, Table 1 and throughout entire article). Isolates from HIV-infected patients that had undergone treatment with nevirapine and/or AZT were tested for susceptibility to nevirapine and AZT. Richman tested for multiple mutations in RT of patients receiving nevirapine and/or AZT in order to determine if different mutations occurred with monotherapy versus combination therapy (abstract). Therefore the claims are anticipated by Richman.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richman as applied to claims 1-13 and 15-18 above, and further in view of Whitcomb (WO 99/61658). The claims have been summarized above. Claims 14 and 19 require that three mutations in HIV-1 RT be tested for in the method. Richman discloses nevirapine resistance mutations of HIV-1 RT: 100, K103N, V106A, Y181C, V108I, Y188L, G190A, 236 and others (abstract, Table 1 and throughout entire article). Isolates from HIV-infected patients that had undergone treatment with nevirapine and/or AZT were tested for susceptibility to nevirapine and AZT. Richman tested for multiple mutations in RT in patients receiving nevirapine and/or AZT in order to determine if

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different mutations occurred with monotherapy versus combination therapy (abstract).

Richman is silent on the exact substitution mutations of HIV-1 RT at certain codons, 236, for example.

However, Whitcomb discloses the common mutations that are known to affect the susceptibility of non-nucleoside inhibitors: P225H and P236L, for example. It would have been obvious to use the mutations disclosed by Whitcomb in the method of Richman. One would have been motivated to use the mutations because Richman discloses the codon at which the mutation takes place, and Whitcomb fills in the missing substitution information. One would have had a reasonable expectation of success that Whitcomb's mutations would have worked in the method of Richman, since both are in the field of detecting mutations that affect drug susceptibility in HIV-1 reverse transcriptase. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

*Conclusion*

7. No claim is allowed. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

*SBC*  
Stacy B. Chen  
September 14, 2004

*James C. Housel*  
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